

## *Review Article*

## Diffusion-Weighted MRI for the Assessment of Liver Fibrosis: Principles and Applications

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The importance of an early identification of hepatic fibrosis has been emphasized, in order to start therapy and obtain fibrosis regression. Biopsy is the gold-standard method for the assessment of liver fibrosis in chronic liver diseases, but it is limited by complications, interobserver variability, and sampling errors. Several noninvasive methods have been recently introduced into clinical routine, in order to detect liver fibrosis early. One of the most diffuse approaches is represented by diffusion-weighted liver MRI. In this review, the main technical principles are briefly reported in order to explain the rationale for clinical applications. In addition, roles of apparent diffusion coefficient, intravoxel incoherent motion, and relative apparent diffusion coefficient are also reported, showing their advantages and limits.

## 1. Introduction

Several chronic hepatic diseases may develop cirrhosis in the liver parenchyma. Hepatic steatosis, iron overload, autoimmune hepatitis, chronic viral hepatitis, sclerosing biliary cholangitis, alcohol, and drugs represent the most frequent causes of liver cirrhosis. All these chronic diseases, after an early phase of inflammation, lead to parenchymal fibrosis, which plays an important role in the development of cirrhosis [1].

Fibrogenesis has been defined as a "wound-healing response that engages a range of cell types and mediators to encapsulate injury" [2]. It consists of a progressive deposition of extracellular matrix proteins, which reduces widening of interstitial spaces and creates distortion of normal hepatic architecture [3]. It has been widely accepted that early recognition of fibrosis is crucial for preventing development of chronic parenchymal disease. New experimental treatments have emphasized the importance of an early identification of fibrogenesis, in order to start therapy and obtain fibrosis regression [4–6].

Biopsy is the gold-standard modality for assessing the degree of fibrosis and for evaluating necrosis or inflammation. However, it is affected by many complications, including bleeding, pneumothorax, and procedure-related death, and could be limited by interobserver variability and sampling errors [3, 7–10]. In addition, liver biopsy is not used in the management of disease, especially when we have to repeat the examination after a short interval of time, as reported by Kim et al. [3].

For this reason, in the past years many noninvasive tests and diagnostic examinations have been introduced into clinical routine in order to detect liver fibrosis early.

The collection of serum markers of fibrosis, namely, fibrotest/fibrosure, has been widely used in the assessment of hepatic fibrosis [3, 11–14]. Serum levels of aptoglobulin,  $\alpha$ 2-macroglobulin,  $\gamma$ -globulin,  $\gamma$ -glutamyl transferase, apolipoprotein, and total bilirubin indicate a score of hepatic fibrosis with relatively good accuracy [12–14].

Other noninvasive modalities include Transient Elastography (TE), Acoustic Radiation Force impulse Imaging (ARFI), Real-Time Elastography (RTE), and Magnetic Resonance Elastography (MRE). Particularly, measurement using TE has been routinely introduced into the assessment of liver fibrosis [15, 16]. This technique is based on the measurement of liver hardness and stiffness. More specifically, a FibroScan test using TE measures the velocity of a vibration wave produced by an ultrasonography-like probe [17]. The time